evidenced by elevated C-reactive protein and low serum albumin) has been established as an independent predictor of survival in patients with metastatic breast cancer. However, the relationship between these systemic inflammatory markers, clinicopathological characteristics and cancer specific survival has not been established in early breast cancer.

Methods: During the period June 2001–May 2008, patients with early breast cancer presenting to two hospitals in the West of Scotland were prospectively included into this study ($n = 959$). Preoperative C-reactive protein, albumin and clinico-pathological data were recorded for each patient. The thresholds for normal C-reactive protein and albumin were taken as <6 mg/l and >43 g/l respectively.

Results: The median follow-up of the survivors was 4.1 years. During this period, 93 patients died of their cancer. On multivariate analysis, tumour size (HR 2.03; 95%CI 1.41–2.91, $P < 0.001$), lymph node status (HR 2.23; 95%CI 1.45–3.41, $P < 0.001$), hormone receptor status (HR 1.58; 95%CI 1.24–2.00, $P < 0.001$) and albumin <43 g/l (HR 1.97; 95%CI 1.28–3.01, $P = 0.002$) were significant independent predictors of cancer-specific survival. Lower serum albumin concentrations (<43 g/l) were associated with deprivation ($P = 0.019$) and significantly poorer 5-year cancer-specific survival (85% vs. 92% $P = 0.005$).

Conclusions: The results of the present study show that lower preoperative albumin concentrations, but not elevated C-reactive protein concentrations, predict cancer-specific survival, independent of clinico-pathologic status in early breast cancer. Albumin may be a useful clinical prognostic factor in these patients.

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O-66 REDUCED MCPH1 EXPRESSION IN BREAST CANCER IS ASSOCIATED WITH REDUCED SURVIVAL IN DUCTAL CARCINOMAS

Julie Richardson [a], Abeer M. Shaaban [b], Mohamed Kamal [a], Ian Ellis [c], Valerie Speirs [a], Andrew Green [c], Sandra M. Bell [a]. [a] *Leeds Institute of Molecular Medicine, University of Leeds, Leeds, UK.* [b] *St James's Institute of Oncology, St. James's University Hospital, Leeds, UK.* [c] *Department of Pathology, Nottingham University Hospitals, UK*

We have investigated the expression pattern of the MCPH1 protein microcephalin and evaluate its prognostic importance in breast cancer. Microcephalin is a damage response protein involved in the regulation of BRCA1 and BRCA2 in the homologous DNA repair pathway. BRCA1 mutations are often associated with basal-like breast cancer. MCPH1 immunohistochemistry was performed on 319 breast cancers and correlated with pathology, survival, ER, PR, HER2, EGFR, CK5/6, CK14 and BRCA1 data.

After performing continuous data analysis mean microcephalin expression decreased with increasing grade, grades 1 and 2 vs. grade 3 ($p < 0.006$). Interestingly mean microcephalin expression was also lower in ER/PR negative ($p < 0.001$) and triple negative cancers ($p < 0.004$). Conversely an association with HER2 positive cancers was also identified ($p < 0.03$). No association was identified with basal markers or BRCA1 cytoplasmic staining.

After dichotomizing the data into low and high microcephalin expression, reduced expression was identified in 29% (93/319) of breast cancers. A weak association with low microcephalin expression was identified with overall survival (OS) $p = 0.1$ in the whole patient series. This was increased in ductal carcinomas alone (HR = 0.6, 95%CI: 0.4–1, $p = 0.054$). Multivariate analysis of ductal carcinomas showed that microcephalin, together with stage, was considered an independent predictor of OS (HR = 0.5, 95%CI: 0.3–0.851, $p = 0.01$).

Microcephalin expression is reduced in 29% of breast cancers, particularly in higher grade tumours and is an independent predictor of OS in ductal carcinomas. Microcephalin may prove to be a useful biomarker for the identification of aggressive breast cancers.

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O-67 ASSESSMENTS OF PROLIFERATION IN BREAST CANCER

M. Sundquist, L. Brudin, A. Kovacs, G. Mathe, G. Tejler, S. Thorstenson. *Kalmar County Hospitals and Sahlgrenska University Hospital, Gothenburg, Sweden*

Background: Proliferation rates of tumour cells provide prognostic and therapy predictive information. Mitotic index (MI), S-phase fraction (SPF) and Ki67/MIB-1 are used to assess proliferation.

Aim: To compare the proliferation assays and explore their correlation.

Patients and methods: MI, SPF and 5-year follow-up data were explored for 670 patients from the hospitals of Kalmar County. MI, Ki67/MIB-1 and 3-year follow-up data for 403 patients from the Sahlgrenska University Hospital were extracted.

Results: MI and Ki67 were both significantly correlated to early recurrence, $p < 0.001$. The optimal correlation between MI and Ki67 was achieved when both were separated in three groups with cut off values for Ki67 of 10 and 30%. Spearman $r = 0.69$, $p < 0.0001$. The 39 early distant recurrences were distributed in the MI group 1–3, group 2–11 and group 3–25 recurrences. Two pts with Ki67 <10% had distant recurrences, 22 with 10–30% and 15 pts in the group of Ki67 < 30%.

The combination of diploidy and low SPF identified pts with the lowest and MI 3 those with the highest risk of distant recurrence.

Conclusion: Mitotic index was superior to Ki67 and SPF to identify pts with inferior prognosis. The cytometric assay was superior to identify pts with the best prognosis. There was a significant correlation between MI and Ki67 when both were stratified into three groups.

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O-68 THE EFFECT OF LYMPHOVASCULAR INVASION (LVI) ON SURVIVAL

R.W. Blamey, M. Sundquist, S. Bianchi, A. Douglas-Jones, I.O. Ellis, A.H.S. Lee, S. Pinder, S. Thorstenson, G.R. Ball, On behalf of the ONCOPOOL Consortium

ONCOPOOL database (n = 17,000) is of primary operable breast cancers in women aged ⩽70, from 12 European Breast Units, treatment in 1990–99.

Method: LVI was regularly measured in 4 units (n = 5195) on H & E staining. Scoring was to positive or negative. 20% were LVI+.

Results:

A. Relation to Nottingham Prognostic Index (NPI). A highly significant rank order, 7% LVI+ lying in Excellent NPI group to 60% in the poor groups.
B. Effect on survival – breast cancer specific (BCS)

	LN STAGE	LVI	n	LN/LVI group	10 year BCS%		p
1	LN Neg	Neg	2359	1	86 ± 1	}	<.000
2	LN Neg	Pos	429	2	78 ± 3		
	LN 1 Pos	Neg	413		80 ± 2	}	=.025
3	LN 1 Pos	Pos	245	3	73 ± 4		
	LN 2-3 Pos	Neg	307		72 ± 3	}	=.25
4	LN 2-3 Pos	Pos	266	4	65 ± 4		
	LN 4+ Pos	Neg	574		69 ± 2	}	<.000
5	LN 4+ Pos	Pos	508	5	44 ± 3		

Conclusion: LVI positivity by its effect on LN stage lowers survival within all Nottingham Prognostic Index (NPI) groups.

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O-69 PREDICTING THE PROBABILITY OF OUTCOME IN BREAST CANCER – A COMPARISON OF DIFFERENT MACHINE LEARNING METHODS

A. Al-allak, R. Leonard, P. Lewis. *Institute of Life Science, School of Medicine, Swansea University, UK*

Introduction: As clinicians we are commonly asked by patients 'what is my chance of surviving breast cancer?' In recent years numerous attempts have been made to utilise both machine learning methods and large datasets to develop new tools to predict survival. The aim of our study was to firstly compare the performance of a number of these models and secondly to introduce a new model that provides a simple means of predicting the probability of survival.

Methods: The Surveillance, Epidemiology, and End Results (SEER) data was used to build a data set of women diagnosed with breast cancer between 1990 and 1997. We used the statistical packages *R* and Weka to generate the models based on tumour size, grade and nodal involvement. Methods applied were: support vector machines, decision trees, boosting, bagging, random forests and Naïve Bayes Decision Tree (NBTree).They were validated using 10-fold cross validation.

Results: A total of 50,895 women were included in the analysis. Each model was generated 10 times, validated and then tested. The best performing model was Random forests with the ability to correctly predict the outcome in 70.56%. The NBTree model was the second best performing model (69.26%) which also provided a probability for ten year survival.

Conclusion: Although the random forests model was the most robust model, from a clinicians point of view, the NBTree model produced a decision tree that can easily be integrated into patient care and that also puts a value on the probability of survival.

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O-70 COMPARISON OF PREDICT AND ADJUVANT! PROGNOSTICATION MODELS FOR EARLY BREAST CANCER IN A UK DATASET

G.C. Wishart, Helen Campbell, E.M. Azzato, D.C. Greenberg, J. Rashbass, C. Caldas, P.D.P. Pharoah. *Cambridge Breast Unit, UK*

Aim: We have recently developed and validated a prognostication model (PREDICT), that predicts overall survival for women treated for early breast cancer in the UK, based on cancer registry data.[1] We have now compared the mortality prediction from PREDICT against Adjuvant! in an independent UK dataset.

Method: 10-Year overall survival (OS) and breast cancer-specific survival (BCSS) data were available for 1065 women treated at the Churchill Hospital in Oxford between 1986 and 1996. 10-Year predictions for OS and BCSS from PREDICT and Adjuvant! were compared with the observed 10-year outcomes for these patients.

Results: Of the 1065 cases, 891 had optimal breast cancer surgery that included radiotherapy following breast conserving surgery and adequate axillary staging. The results are shown in the Table.

	Actual mortality	PREDICT	Adjuvant!
All cause mortality	234	199	191
Breast cancer specific mortality	161	151	133

Conclusion: In this UK dataset, PREDICT performed better than Adjuvant! for both OS and BCSS. For breast cancer specific mortality, PREDICT's estimate was within 1% of actual mortality compared to a 3% difference for Adjuvant! Further comparisons in other datasets are ongoing.

Reference:

1. Wishart GC, Azzato EM, Pharoah PDP, Greenberg DC, Rashbass O, Kearins O, et al. PREDICT: a new UK prognostic model that predicts survival following surgery for invasive breast cancer. *Breast Cancer Res* 2010;**12**(1):R1.

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O-71 RESCORING OF GRADE AND RE-EVALUATION OF THE NOTTINGHAM PROGNOSTIC INDEX (NPI) USING COMPONENTS OF ELSTON ELLIS GRADE AND ADDING LYMPHO-VASCULAR INVASION

R.W. Blamey, G.R. Ball, A.H.S. Lee, S. Bianci, A. Green, B. Hornmark-Stanstam, T. Kuukasjarvi, S. Pinder, F. Rank, I.O. Ellis. *Nottingham City Hospital and the ONCOPOOL Consortium, UK*